

Enhanced Assessment of the Health Status of Vaccine Protected Personnel At-Risk to Multiple Biowarfare Agents Using a Novel, Web-Based Clinical Data Management System (CDMS)

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BACKGROUND

The Special Immunization Program (SIP) Clinic at the U. S. Army Medical Research Institute of Infectious Diseases (USAMRIID) provides investigational vaccines developed as potential biological defense products for Armed Forces personnel. These investigational products are used as adjunct protection for potential occupational exposures to at risk workers at USAMRIID under strict Food and Drug Administration (FDA) clinical research regulations. The program offers unique immunization and occupational health services for in-house laboratory staff, as well as for deployed military personnel and other Federal employees who are at risk of exposure to certain biological threat agents.

The SIP has a requirement for a Clinical Data Management System (CDMS) to collect, store, retrieve, and archive protocol specific clinical trials data in a manner that is efficient, cost effective, and compliant with all FDA regulations including 21 CFR Part 11. However, in addition to the normally expected attributes of other clinical trials, the SIP possesses a number of distinctive characteristics that demand unique solutions. Unlike most clinical trials in which participation in one study would exclude that subject from participation in another study, the SIP has subjects who are enrolled in as many as six studies simultaneously. Generally, the purpose for participation in concurrent studies is to provide protection for potential occupational exposures to multiple agents, even if conclusions drawn from these studies may be confounded by dependent variables among protocols that become inextricable. Regardless, the results of this practice introduce a construct singularly unique to the administration of these studies. An immunization on one trial becomes a concomitant medication for all other trials in which the subject is enrolled. A single adverse event must be recorded as many times as the number of protocols on which the subject is participating. All data from a single annual physical must be documented on protocol specific records for every protocol on which there is enrollment.

In paper-based, trials management, all data are recorded contemporaneously onto Case Report Forms (CRFs) or onto Source Documents that are later transcribed onto CRFs. CRFs are study specific, always containing the study title, protocol number, and PI name and signature block on each page in order to maintain GCP compliance. Together, the unique qualities of the SIP and the nature of paper-based, GCP compliant trials conspire to multiply the workload requirements for the conduct of SIP protocols. Although there are only approximately 900 volunteers in this entire program, the burden of conducting these trials is equivalent to 900 times the average number of protocols on which each subject is enrolled. If subjects are enrolled 3.5 protocols, on average, then the subject burden for these studies is over 3000.

The first requirement for a CDMS is to electronically manage clinical data in an FDA compliant fashion. However, it is strongly desired for this database to facilitate data management such that process improvements in the conduct of trials become more efficient, more cost effective, and that facilitates the work flow of the clinic. The Office of Regulatory Affairs (formerly the Office of Product Development and Regulatory Affairs) accepted the challenge of identifying and implementing a database that meets all the above requirements. With the full support and collaboration of the Medical Division, funding was sequestered to initiate a project to identify, contract, and implement a Commercial-Off-the-Shelf (COTS) CDMS that satisfies requirements of the SIP, the sponsor and the FDA. The present discussion details the rationale and generation of a novel database design that was development in-house by one of the authors. The database design presented here was provided to the contractor who reduced it to practice for implementation.

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NOVEL DATABASE DESIGN

Traditional (Figure 1) and our novel (Figure 2) database designs to collect, store, retrieve and report data from clinical trials are shown below. In traditional CDMS design, the database is configured in a way that is consistent with the design used in most clinical trials currently conducted within the pharmaceutical industry. Data is first collected in a source document as a portion of a patient's medical record. All or part of the data contained within this source document is then transcribed onto study specific Case Report Forms (CRFs) that are maintained in study specific paper files. Alternatively, data is collected directly onto CRFs. Even for data that is common to all trials, CRFs must be filled out for each and every trial. Data entry clerks enter information contained in the CRFs through a double data entry process via keyboard into a study specific, electronic silo, a portion of the database that contains only study specific information. Again, data common to all trials that are repeatedly transcribed onto different CRFs must be entered into the database separately for each of the separate trials. Protocols are stand-alone and generally non-interactive.

In our novel design, all data collected within the patient records are entered directly into a single database file called the SIP Master Record. After data entry, data that is specific to one or more protocols is automatically copied from the SIP Master Record to study specific, electronic silos set up for each of the actual protocols (1,2, n). This transfer is automatic per encoded commands that are triggered by the protocol number, dates the protocol is open, enrollment dates of subject, dates of data collection, and study specific information. Data entry and editing occurs in the SIP Master Record area only, not in the individual protocol silos. CRF-like reports having protocol and protocol identifiers are then printed out for each study to allow quality assurance of the data and for archiving to study-specific paper files, if desired. When a study is closed, QA'd and locked, it is moved offline and archived as an electronic file containing all data and meta-data related to that study.

FIGURE 1

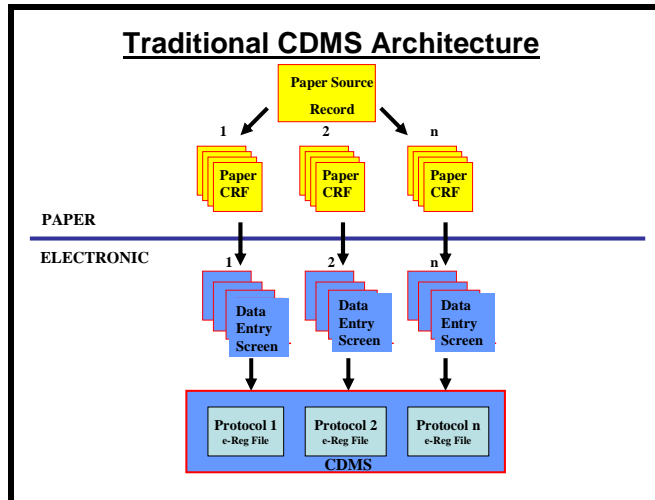
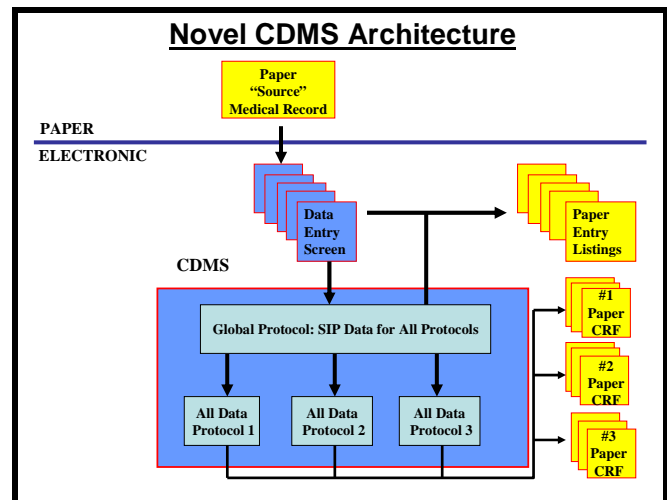


FIGURE 2



CONCLUSION

The novel database design presented here best satisfies the requirements of SIP and has advantages that outstrip other options. The current paper-based process practiced by the SIP that follows the more traditional CDMS design is extraordinarily inefficient and poses considerable regulatory risks, since the staff has great difficulty in keeping pace with the CRF transcription workload. Overall, the new database-assisted approach should lower regulatory risk by producing protocol specific records in a more contemporaneous and accurate manner. This design delivers a cost-effective, time-efficient CDMS that is compliant with FDA regulations, while meeting the unique requirements of the SIP. As this design is fully implemented to all ongoing and new clinical trials, significant savings in time, energy and funding requirements are expected. Moreover, it will allow real-time assessment of the health status of immunized personnel at risk to exposure to biological warfare threat agents for enhanced Force Protection.